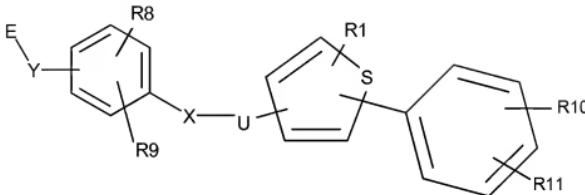


Amendments to the Claims

What is claimed is:

1. (Canceled)
2. (Canceled)
3. (Canceled)
4. (Currently Amended) A compound of the Formula I:



And/or-stereoisomers, pharmaceutically acceptable salts, solvates and hydrates thereof, wherein:

- (a) R1 is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>8</sub> alkyl, C<sub>1</sub>-C<sub>8</sub> alkenyl, phenyl, , and C<sub>3</sub>-C<sub>6</sub> cycloalkylaryl-C<sub>0</sub>-2-alkyl, and wherein C<sub>1</sub>-C<sub>8</sub> alkyl is optionally substituted with from one to three substituents independently selected from R1'; and further wherein C<sub>1</sub>-C<sub>8</sub> alkenyl, phenyl, , and C<sub>3</sub>-C<sub>6</sub> cycloalkylaryl-C<sub>0</sub>-2-alkyl, are each optionally substituted with from one to three substituents independently selected from R2;
- (b) R1' are each independently selected from the group consisting of hydroxy, cyano, nitro, halo, oxo, C<sub>1</sub>-C<sub>6</sub> alkyl-COOR12, C<sub>1</sub>-C<sub>6</sub> alkoxy, C<sub>1</sub>-C<sub>6</sub> haloalkyl, C<sub>1</sub>-C<sub>6</sub> haloalkyloxy, C<sub>3</sub>-C<sub>7</sub> cycloalkyl, aryloxy, aryl-C<sub>1</sub>-4-alkyl, C(O)R13, COOR14, OC(O)R15, OS(O)R16, N(R17)<sub>2</sub>, NR18C(O)R19, NR20SO<sub>2</sub>R21, SR22, S(O)R23, S(O)<sub>2</sub>R24, and S(O)<sub>2</sub>N(R25)<sub>2</sub>; R12, R13, R14, R15, R16, R17, R18, R19, R20, R21, R22, R23, R24 and R25 are each independently selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl and aryl;
- (c) R2, R26, R27, R28, and R31 are each independently selected from the group consisting of hydrogen, hydroxy, cyano, nitro, halo, oxo, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkyl

COOR12, C<sub>1</sub>-C<sub>6</sub> alkoxy, C<sub>1</sub>-C<sub>6</sub> haloalkyl, C<sub>1</sub>-C<sub>6</sub> haloalkyloxy, C<sub>3</sub>-C<sub>7</sub> cycloalkyl, aryloxy, aryl-C<sub>0</sub>-4-alkyl, heteroaryl, heterocycloalkyl, C(O)R13, COOR14, OC(O)R15, OS(O)R16, N(R17)<sub>2</sub>, NR18C(O)R19, NR20SO<sub>2</sub>R21, SR22, S(O)R23, S(O)<sub>2</sub>R24, and S(O)<sub>2</sub>N(R25)<sub>2</sub>;

- (d) X is O;
- (e) U is an aliphatic linker;
- (f) Y is selected from the group consisting of C, O, S, NH and a single bond;
- (g) E is C(R3)(R4)A or A and wherein
  - (i) A is selected from the group consisting of carboxyl, , C<sub>1</sub>-C<sub>6</sub> alkylnitrile, carboxamide, sulfonamide and acylsulfonamide; wherein sulfonamide, and acylsulfonamide are each optionally substituted with from one to two groups independently selected from R<sup>7</sup>;
  - (ii) each R<sup>7</sup> is independently selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>6</sub> haloalkyl, aryl C<sub>0</sub>-C<sub>4</sub> alkyl and C<sub>1</sub>-C<sub>6</sub> alkyl;
  - (iii) R3 is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>5</sub> alkyl, and C<sub>1</sub>-C<sub>5</sub> alkoxy; and
  - (iv) R4 is selected from the group consisting of H, C<sub>1</sub>-C<sub>5</sub> alkyl, C<sub>1</sub>-C<sub>5</sub> alkoxy, aryloxy, C<sub>3</sub>-C<sub>6</sub> cycloalkyl, and aryl C<sub>0</sub>-C<sub>4</sub> alkyl, and R3 and R4 are optionally combined to form a C<sub>3</sub>-C<sub>4</sub> cycloalkyl, and wherein alkyl, alkoxy, cycloalkyl and aryl-alkyl are each optionally substituted with one to three each independently selected from R26; with the proviso that when R1 is C<sub>1</sub>-C<sub>8</sub> alkyl, Y is in a para substituted position with relation to X, and X is selected from the group consisting of a bond and O, then R4 is selected from the group consisting of C<sub>1</sub>-C<sub>5</sub> alkoxy, aryloxy, and arylC<sub>0</sub>-C<sub>4</sub> alkyl; with the additional proviso that when R1 is C<sub>1</sub>-C<sub>8</sub> alkyl, Y is in a para substituted position with relation to X, X is S, and U is optionally substituted methylene, then R4 is selected from the group consisting of C<sub>1</sub>-C<sub>5</sub> alkoxy, aryloxy, and arylC<sub>0</sub>-C<sub>4</sub> allyl;
- (h) R8 is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> alkyl enyl, and halo;
- (i) R9 is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> alkyl enyl, halo, aryl-C<sub>0</sub>-C<sub>4</sub> alkyl, , C<sub>1</sub>-C<sub>6</sub> allyl, and OR29, and wherein aryl-C<sub>0</sub>-C<sub>4</sub> alkyl are

each optionally substituted with from one to three independently selected from R27; R29 is selected from the group consisting of hydrogen and C<sub>1</sub>-C<sub>4</sub> alkyl;

(j) R10, R11 are each independently selected from the group consisting of hydrogen, hydroxy, cyano, nitro, halo, oxo, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkyl-COOR12'', C<sub>1</sub>-C<sub>6</sub> alkoxy, C<sub>1</sub>-C<sub>6</sub> haloalkyl, C<sub>1</sub>-C<sub>6</sub> haloalkyloxy, C<sub>3</sub>-C<sub>7</sub> cycloalkyl, aryl-C<sub>0</sub>-C<sub>4</sub>-alkyl, aryl-C<sub>1</sub>-C<sub>4</sub>-heteroalkyl, heteroaryl-C<sub>0</sub>-C<sub>4</sub>-alkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkylaryl-C<sub>0</sub>-C<sub>2</sub>-alkyl, aryloxy, C(O)R13', COOR14', OC(O)R15', OS(O)R16', N(R17')<sub>2</sub>, NR18'C(O)R19', NR20'SO<sub>2</sub>R21', SR22', S(O)R23', S(O)<sub>2</sub>R24', and S(O)<sub>2</sub>N(R25')<sub>2</sub>; and wherein aryl-C<sub>0</sub>-C<sub>4</sub>-alkyl, aryl-C<sub>1</sub>-C<sub>4</sub>-heteroalkyl, heteroaryl-C<sub>0</sub>-C<sub>4</sub>-alkyl, and C<sub>3</sub>-C<sub>6</sub> cycloalkylaryl-C<sub>0</sub>-C<sub>2</sub>-alkyl are each optionally substituted with from one to three independently selected from R28; and

(k) R12', R12'', R13', R14', R15', R16', R17', R18', R19', R20', R21', R22', R23', R24', and R25' are each independently selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl and aryl.

④.

5. (Withdrawn) A compound as claimed by any one of Claims 1 through 4 wherein X is -O-.

6. (Withdrawn) A compound as claimed by any one of Claims 1 through 4 wherein X is -S-.

7. (Currently amended) A compound as claimed by Claim 1 Claim 4 wherein R4 is selected from the group consisting of C<sub>1</sub>-C<sub>5</sub> alkoxy, aryloxy, and arylC<sub>0</sub>-C<sub>4</sub> alkyl.

8. (Currently amended) A compound as claimed by Claim 2 Claim 4 wherein Y is O.

9. (Previously Presented) A compound as claimed by Claim 7 wherein Y is C.

10. (Previously Presented) A compound as claimed by Claim 7 wherein Y is S.

11. (Currently amended) A compound as claimed by any one of Claims 1 through Claim 4 wherein E is C(R3)(R4)A.

12. (Previously Presented) A compound as claimed by Claim 11 wherein A is carboxyl.

13. (Currently amended) A compound as claimed by Claim 2 Claim 4 -wherein R1 is H.

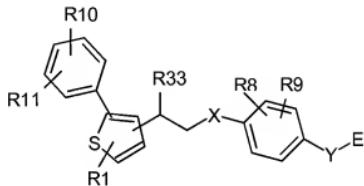
14. (Previously Presented) A compound as claimed by Claim 13 wherein A is COOH and R1 is H.

15. (Previously Presented) A compound as claimed by Claim 14 wherein R10 is haloalkyl.
16. (Previously Presented) A compound as claimed by Claim 11 wherein R10 is CF<sub>3</sub>.
17. (Previously Presented) A compound as claimed by Claim 14, wherein R10 is haloalkyloxy.
18. (Currently Amended) A compound as claimed by Claim 5 Claim 4 wherein R10 and R11 are each independently selected from the group consisting of hydrogen, halo, oxo, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkyl-COOR12'', C<sub>1</sub>-C<sub>6</sub> alkoxy, C<sub>1</sub>-C<sub>6</sub> haloalkyl, and C<sub>1</sub>-C<sub>6</sub> haloalkyloxy.
19. (Currently Amended) A compound as claimed by Claim 4 Claim 5 wherein R10 is selected from the group consisting of C<sub>3</sub>-C<sub>7</sub> cycloalkyl, aryl-C<sub>0</sub>-4-alkyl, aryl-C<sub>1</sub>-4-heteroalkyl, heteroaryl-C<sub>0</sub>-4-alkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkylaryl-C<sub>0</sub>-2-alkyl, and aryloxy.
20. (Currently Amended) A compound as claimed by Claim 4 Claim 5 wherein R8 and R9 are each independently selected from the group consisting of hydrogen and C<sub>1</sub>-C<sub>3</sub> alkyl.
21. (Currently Amended) A compound as claimed by Claim 4 Claim 5 wherein R3, and R4 are each independently selected from the group consisting of C<sub>1</sub>-C<sub>2</sub> alkyl.
22. (Previously Presented) A compound as claimed by Claim 11 wherein R3, and R4 are each independently selected from the group consisting of hydrogen and C<sub>1</sub>-C<sub>2</sub> alkyl.
23. (Withdrawn) A compound as claimed by Claim 6, wherein X-U is optionally substituted -S(CH<sub>2</sub>)<sub>2</sub>.
24. (Previously Presented) A compound as claimed by Claim 11 wherein U is C<sub>1</sub>-C<sub>3</sub> alkyl.
25. (Original) A compound as claimed by Claim 24 wherein U is saturated.
26. (Withdrawn) A compound as claimed by Claim 24, wherein U is substituted with C<sub>1</sub>-C<sub>3</sub> alkyl.
27. (Withdrawn) A compound as claimed by Claim 24, wherein U is substituted with arylC<sub>1</sub>-C<sub>4</sub>alkyl.

28. (Withdrawn) A compound as claimed by Claim 24 wherein one carbon of the U group is replaced with an  $-O-$ .

29. (Previously Presented) A compound as claimed by Claim 11 wherein R1 is phenyl.

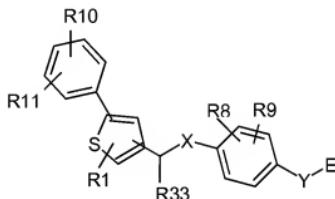
30. (Withdrawn) A compound as claimed by Claim 11 represented by the following Structural Formula II:



wherein R33 is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>3</sub> alkyl, and arylC<sub>0</sub>-C<sub>4</sub> alkyl.

31. (Withdrawn) A compound as claimed by Claim 30 wherein R33 is arylC<sub>1</sub>-C<sub>4</sub> alkyl.

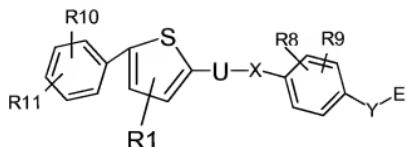
32. (Withdrawn) A compound as claimed by Claim 11 represented by the



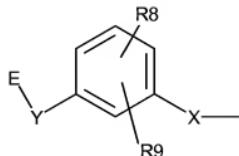
following Structural Formula III:

R33 is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>3</sub> alkyl, and arylC<sub>0</sub>-C<sub>4</sub> alkyl.

33. (Previously Presented) A compound as claimed by Claim 11 represented by the following Structural Formula IV:



34. (Previously Presented) A compound as claimed by Claim 11 wherein the



headpiece of Formula I is:

35. (Previously Presented) A compound as claimed by Claim 11 wherein R4 is selected from the group consisting of C<sub>1</sub>-C<sub>5</sub> alkyl, C<sub>1</sub>-C<sub>5</sub> alkoxy, aryloxy, C<sub>3</sub>-C<sub>6</sub> cycloalkyl, and aryl C<sub>0</sub>-C<sub>4</sub> alkyl, and wherein alkyl, alkoxy, cycloalkyl and aryl-alkyl are each optionally substituted with one to three each independently selected from R26.

36. (Currently Amended) A compound as claimed by Claim 4 Claim 5 wherein E is C(R3)(R4)A.

37. (Previously Presented) A compound as claimed by Claim 6 wherein A is COOH.

38. (Withdrawn) A compound as claimed by Claim 1, wherein the compound is selected from the group consisting of (2-Methyl-4-{2-[3-methyl-5-(4-trifluoromethyl-phenyl)-thiophen-2-yl]-propylsulfanyl}-phenoxy)-acetic acid, (2-Methyl-4-{2-[3-methyl-5-(4-trifluoromethyl-phenyl)-thiophen-2-yl]-propylsulfanyl}-phenoxy)-acetic acid, 3-(2-Methyl-4-{2-[3-methyl-5-(4-trifluoromethyl-phenyl)-thiophen-2-yl]-propoxy}-phenyl)-propionic acid, and (3-{2-[3-Methyl-5-(4-trifluoromethyl-phenyl)-thiophen-2-yl]-propoxy}-phenyl)-acetic.

39. (Withdrawn) A compound as claimed by Claim 1 that is (3-{2-[3-Methyl-5-(4-trifluoromethyl-phenyl)-thiophen-2-yl]-propoxy}-phenyl)-acetic.

40. (Currently Amended) A compound as claimed by Claim 1 Claim 4 -wherein the compound is selected from the group consisting of

Compound	Name
	3-{2-Methyl-4-[5-(4-trifluoromethyl-phenyl)-thiophen-2-ylmethoxy]-phenyl}-propionic acid
	3-{2-Methyl-4-[3-phenyl-5-(4-trifluoromethyl-phenyl)-thiophen-2-ylmethoxy]-phenyl}-propionic acid
	3-{4-[3,5-Bis-(4-trifluoromethyl-phenyl)-thiophen-2-ylmethoxy]-2-methyl-phenyl}-propionic acid

41. (Currently Amended) A compound as claimed by ~~Claim 1~~ **Claim 4** which is 3-{2-Methyl-4-[5-(4-trifluoromethyl-phenyl)-thiophen-2-ylmethoxy]-phenyl}-propionic acid.

42. (Previously Presented) A compound as claimed by **Claim 11** which is the S conformation.

43. (Previously Presented) A compound as claimed by **Claim 11** which is the R conformation.

44. (Previously Presented) A pharmaceutical composition, comprising as an active ingredient, at least one compound as claimed by **Claim 11** together with a pharmaceutically acceptable carrier or diluent.

45. (Cancel)

46. (Previously Presented) A method of treating diabetes mellitus in a mammal, comprising the step of administering to the mammal in need thereof, a therapeutically effective amount of at least one compound of Claim 11.
47. (Previously Presented) A method of treating Metabolic syndrome in a mammal, comprising the step of administering to the mammal in need thereof a therapeutically effective amount of at least one compound of Claim 11.
48. (Previously Presented) A method of selectively modulating a PPAR delta receptor comprising administering a compound as claimed by Claim 11 to a mammal in need thereof.
49. (Cancel)
50. (Previously Presented) A method of treating atherosclerosis in a mammal, comprising the step of administering to the mammal in need thereof a therapeutically effective amount of at least one compound of Claim 11.
51. (Previously Presented) A method for treating or preventing the progression of cardiovascular disease in a mammal in need thereof comprising administering a therapeutically effective amount of a compound as Claimed by Claim 11.
52. (Original) A method as claimed by Claim 51 wherein the mammal is diagnosed as being in need of such treatment.
53. (Previously Presented) A method of treating arthritis in a mammal, comprising the step of administering to the mammal in need thereof, a therapeutically effective amount of at least one compound as claimed by Claim 11.
54. (Previously Presented) A method of treating demyelinating disease in a mammal, comprising the step of administering to the mammal in need thereof, a therapeutically effective amount of at least one compound as claimed by Claim 11.
55. (Previously Presented) A method of treating inflammatory disease in a mammal, comprising the step of administering to the mammal in need thereof, a therapeutically effective amount of at least one compound as claimed by Claim 11.
56. (Previously Presented) A method as claimed by Claim 53 wherein such mammal is diagnosed as being in need of such treatment.
57. (Previously Presented) A compound as claimed by Claim 11 for use as a pharmaceutical.

58. (Previously Presented) A compound as claimed by Claim 11 wherein the compound is radiolabeled.
59. (Canceled)
60. (Canceled)